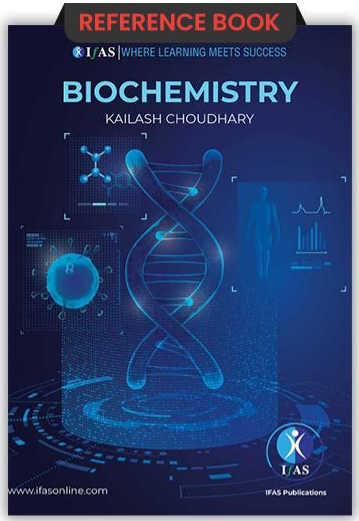
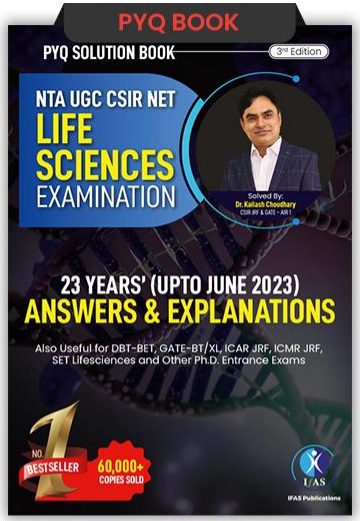
खोल दो पंख मेरे कहता है परिंदा,
अभी तो और उड़ान बाकी है,
ज़मीन नहीं है मंज़ील मेरी,
अभी तो पूरा आसमान बाकी है।

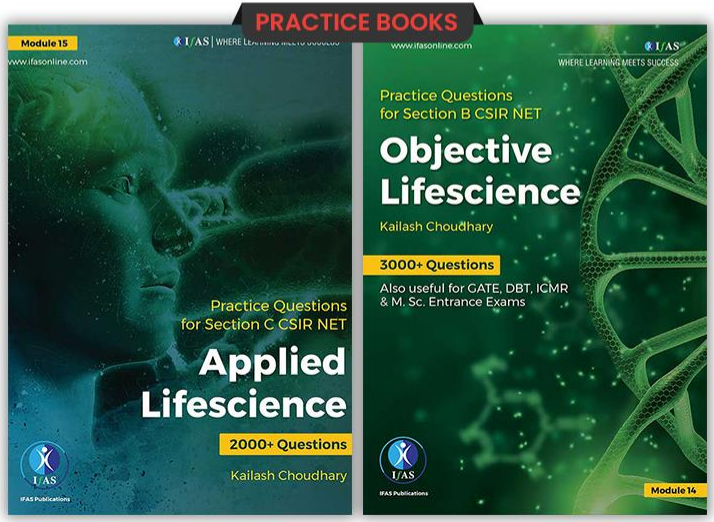
CSIR NET – Life Science

Unit 1: Biochemistry

02 Molecular Interactions

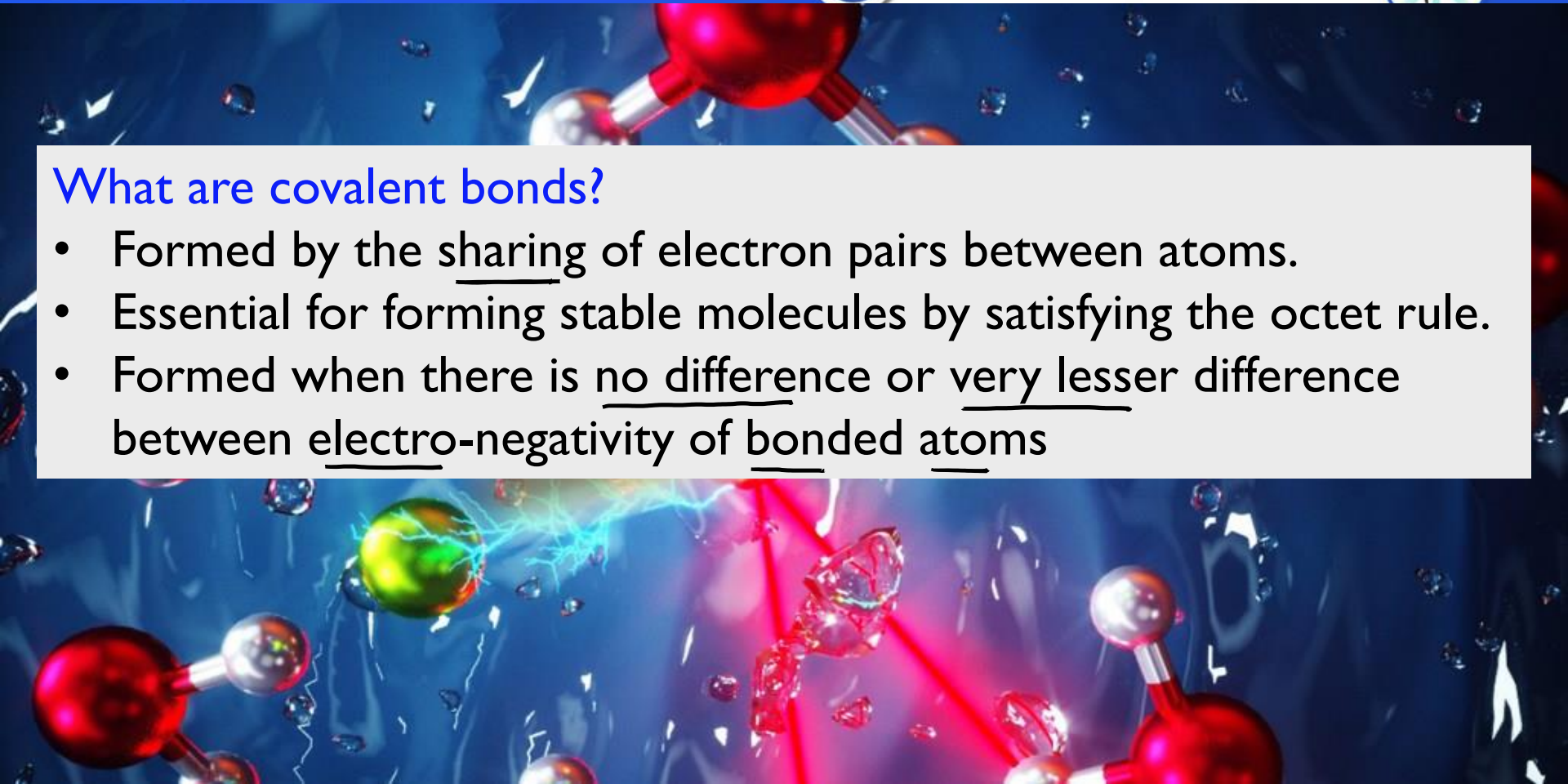






Points to be covered in this Lecture

- Covalent Bonds
- Ionic Bonds and Electrostatic Interactions
- Hydrogen Bonds
- Hydrophobic Interactions
- Vander wall Interactions
- What is molecule?

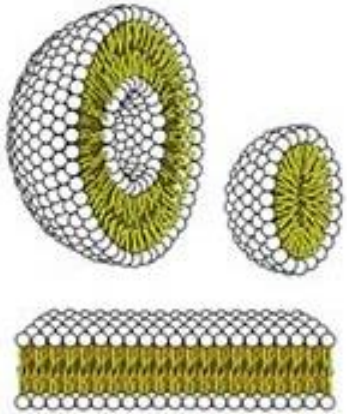


What are covalent bonds?

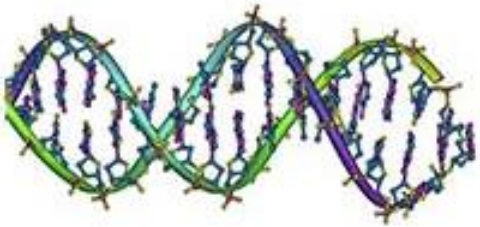
- Formed by the sharing of electron pairs between atoms.
- Essential for forming stable molecules by satisfying the octet rule.
- Formed when there is no difference or very lesser difference between electro-negativity of bonded atoms

Fundamental to the primary (basic) structure to all bio-molecules.

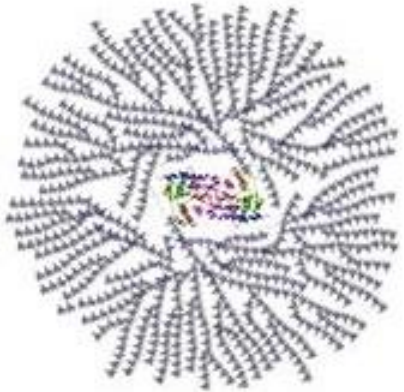
- Ester bond of lipids → Acid & Alcohol
- Phosphodiester bond of nucleic acids → Alcohol + Acid + Alcohol (3' Ⓟ 5')
- Glycosidic bonds of carbohydrates → Aldehyde (Ketone) + Alcohol
- Peptide bond of protein → Acid + Amino group.



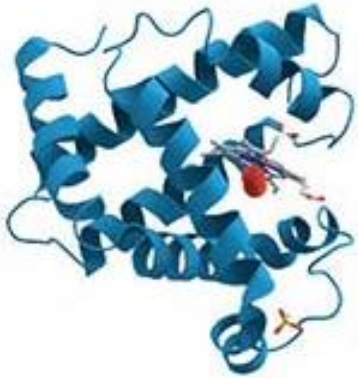
LIPIDS



NUCLEIC ACIDS

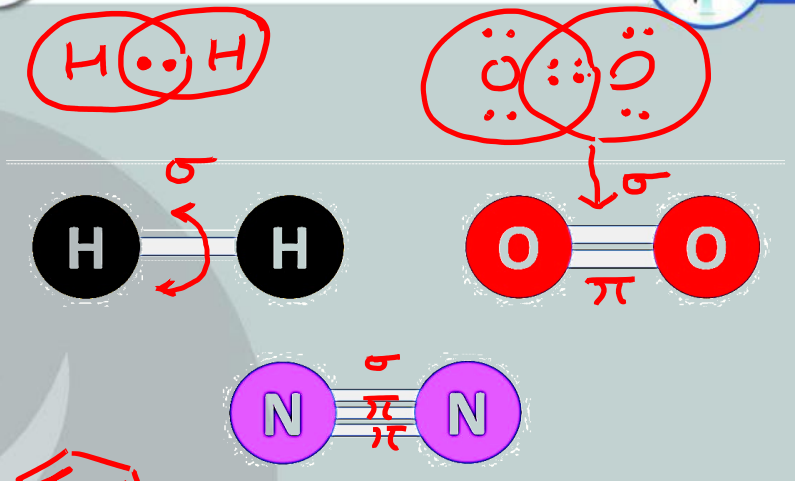


CARBOHYDRATES



PROTEINS

Single, double and triple covalent bond



Single bonds (sigma bonds) allow free rotation
- only one pair of electron is shared

Double bonds (one sigma, one pi) restrict rotation
- Two pair of electron are shared

Triple bonds are even stronger and more rigid.
- three pair of electron are shared

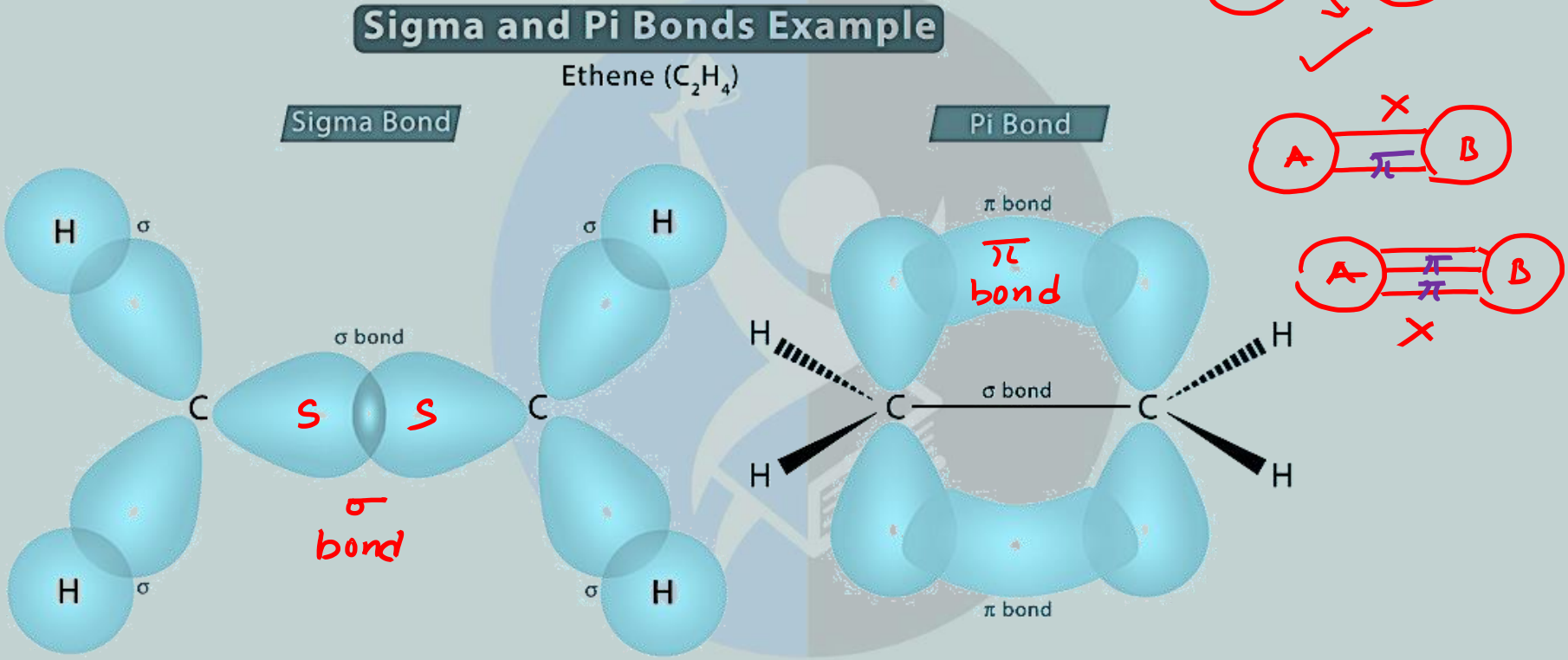
Energy $\equiv > = >$ —

CH_3-CH_3

$CH_2=CH_2$

$CH\equiv CH$

Pi-orbital overlap: Leads to Restricted rotation



Orbital Hybridization

sp^3 hybridization: Tetrahedral molecules, 109.5°

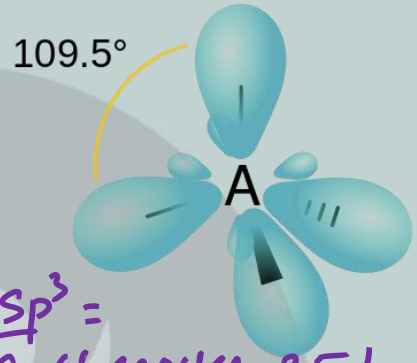
eg methane, H_2O (104°)

sp^2 hybridization: planar molecules, 120°

eg Ethene

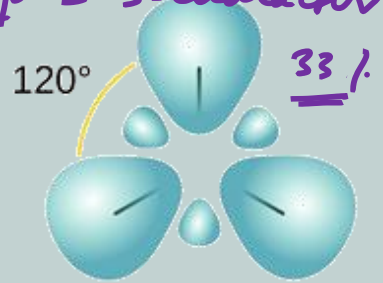
sp hybridization: linear molecules, 180°

Examples: Methane (sp^3), Ethene (sp^2), acetylene (sp).

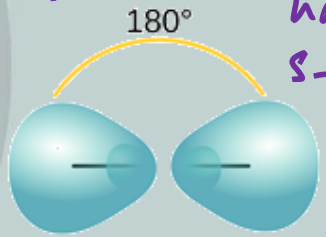


sp^3 = S-character = 25%

sp^2 = S-character



33%



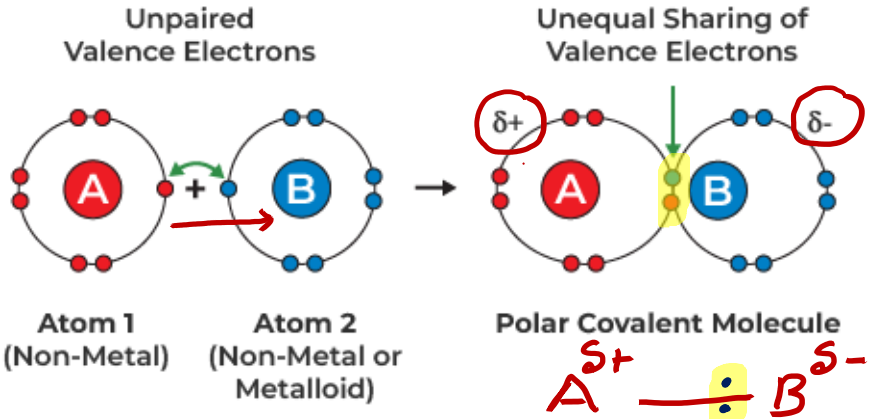
Tripple bond has maximum S-character (50%) ✓

↓

most stable

Polar Covalent Bonds:

- There is difference in electronegativity between bonded atoms. O–H, N–H
- Polar bonds result in partial charges



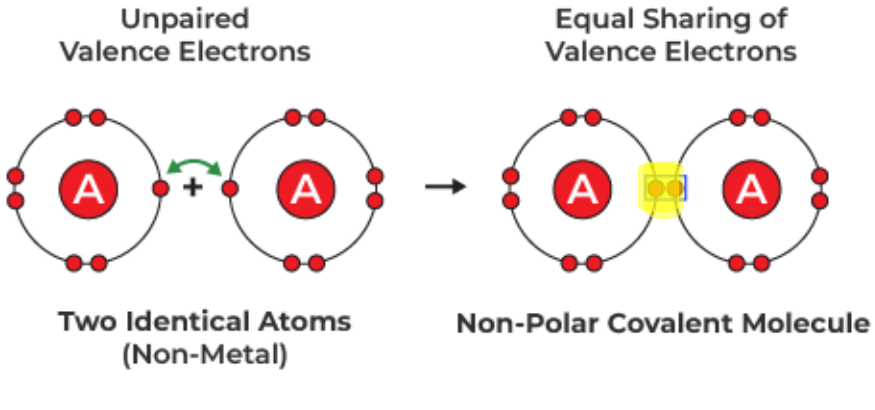
eg Glucose, amino acid, H_2O, NH_3

Like Dissolve in Like

Non-polar Covalent Bonds:

- Involve equal sharing of electrons.

eg H–H, O–O, N–N
C–H



eg Fatty acid, oil
O_2, CO_2, N_2, H_2
Steroids

Factor affecting Bond strength

200-500 KJ/mole [45 – 120 K.cal/mole]

1. Size of Atoms

Small : more strength
Large : Lesser strength
eg H–H > S–S

2. Polarity of Bonds

Polar = more strength
Non-polar = lesser strength
eg O–H > C–H
461 415

Type of bond	Bond energy (kJ/mol)	Type of bond	Bond energy (kJ/mol)
Single Covalent bond		Double Covalent bond	
S-S	214	P=O	502
N-O	222	C=C	611
C-S	260	C=N	615
C-N	293	C=O	712
S-H	340		
C-C	350	Triple Covalent bond	
C-O	350	C ≡ C	816
N-H	390	N ≡ N	930
C-H	415		
P-O	420		
H-H	436		
O-H	461		

Apply Your Mind

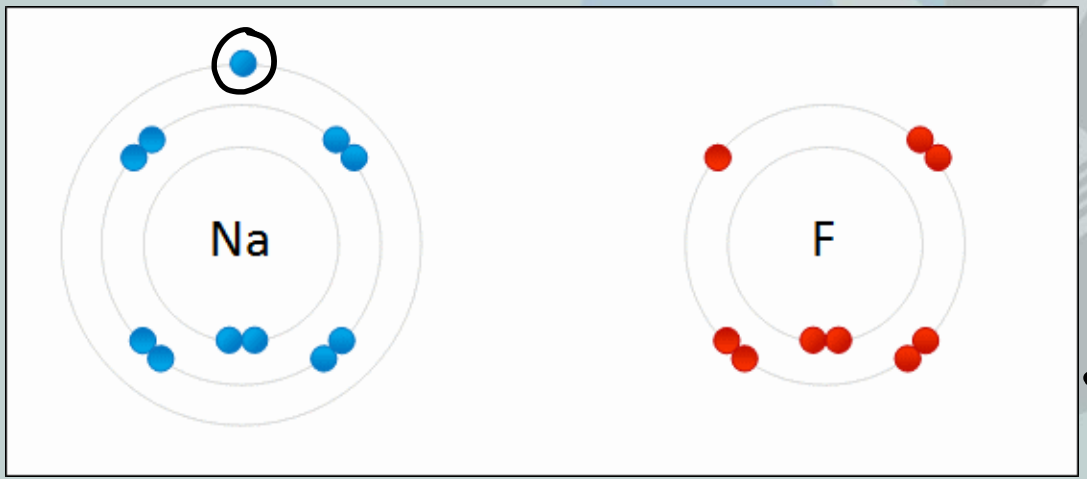
Which of the following is expected to have strongest covalent bond?

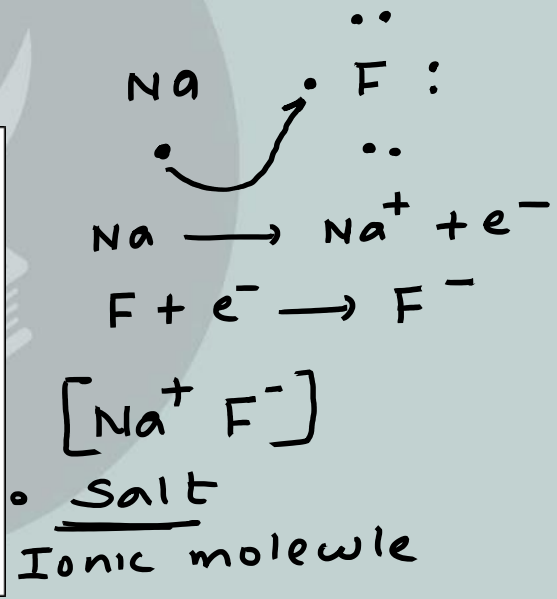
(1) H–H ← small size
(2) C–C
(3) S–S
(4) N–N

Non-polar

What are ionic bonds/interactions?

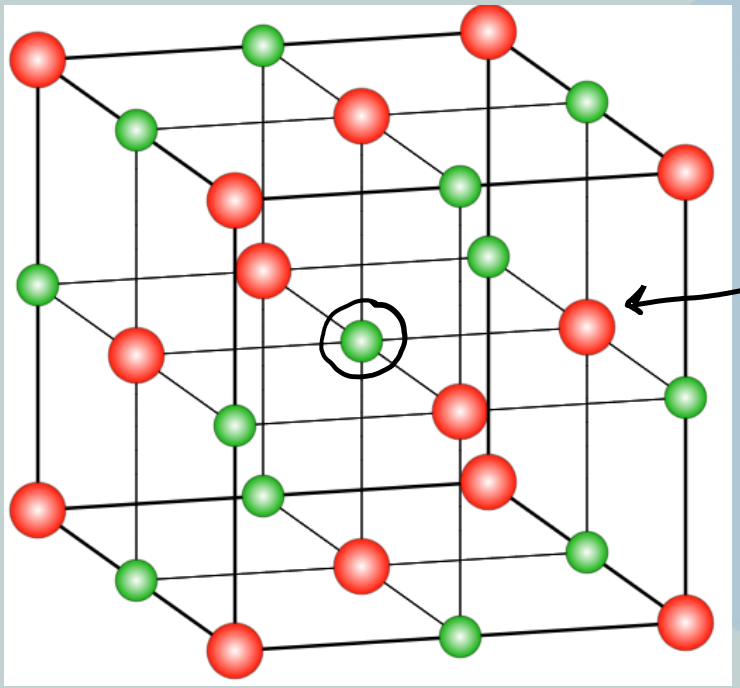
- Formed between atoms when there is large difference in electronegativity.
- Transfer of electrons from electropositive atoms to electronegative atoms





Ionic Substance (Salts) forms Crystal Structure

Cubic structure (FCC) of NaCl where each Na^+ is surrounded by 6 Cl^-



Cl^- is surrounded by 6 Na^+

Force and energy of ionic bonds?

$$E = \frac{kQ_1Q_2}{R}$$

$$F = \frac{K q_1 q_2}{r^2 D}$$

$$E = F \times r$$

$$E = \frac{K q_1 q_2}{r \cdot D}$$

D = Dielectric constant of medium

air or vaccum

D = 1

Ionic bond can be stronger than Co-valent bond in vaccum or air

D = 1

But weaker in biological system (water D = 80)

air/vacuum = 600 - 1000 kcal/mole

Non-polar Env^{r} : 40-50 K cal/mole

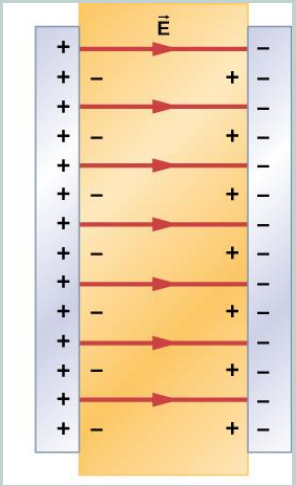
Polar Env^{r} : 3-5 K cal/mole

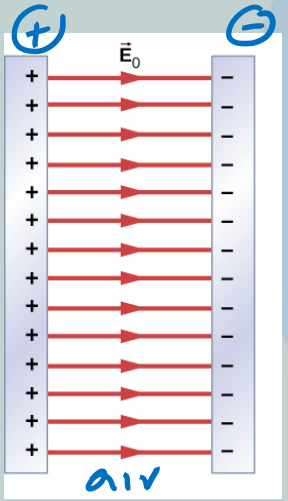
40-50 kcal/mole

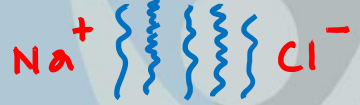
What is dielectric constant:

Solvent (water, glycerol)

It is the ratio of the charge stored in an insulating material placed between two metallic plates to the charge that can be stored when the insulating material is replaced by vacuum or air







High D = water, DMSO, glycerol

Low D = Acetone, Petroleum ether, chloroform

Lowest D = air or vacuum.

$$E \propto \frac{1}{D}$$

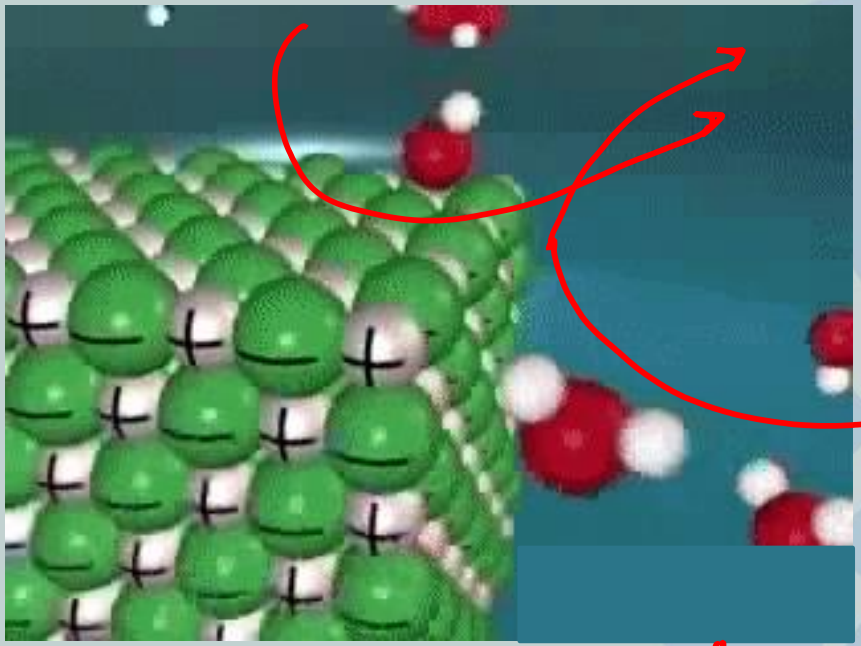
Charge separation

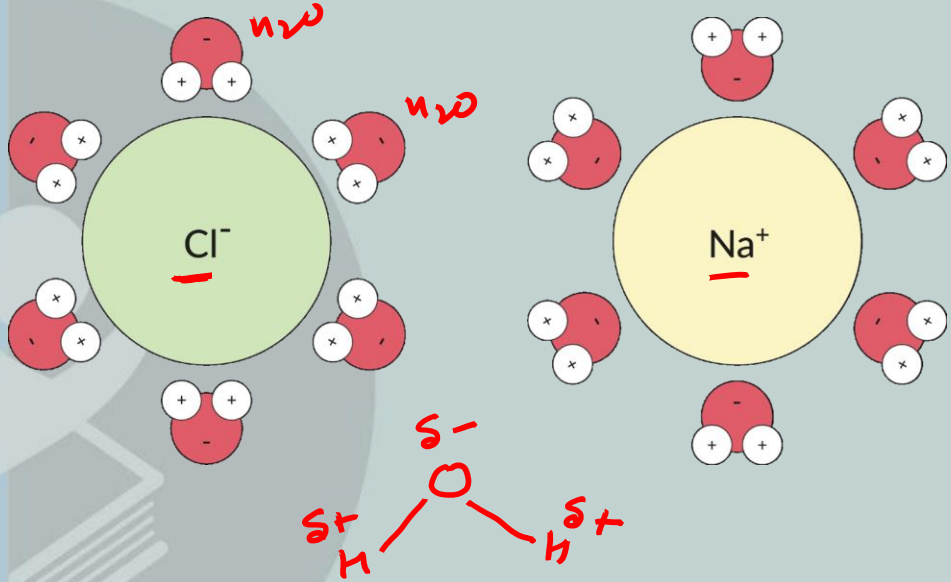
More easily salt dissolve

Ionic bonds

The energy of electrostatic interaction of the same system in water is 80 times lesser than in air or vacuum

Why solubility of $NaCl$ is greater in water than ethanol?



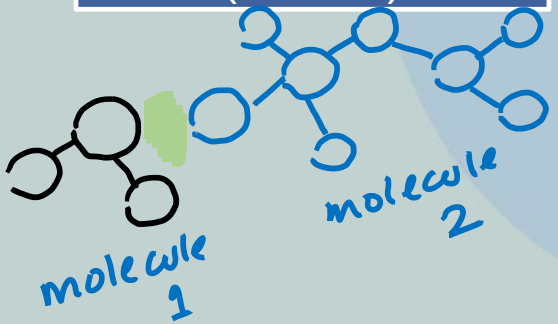


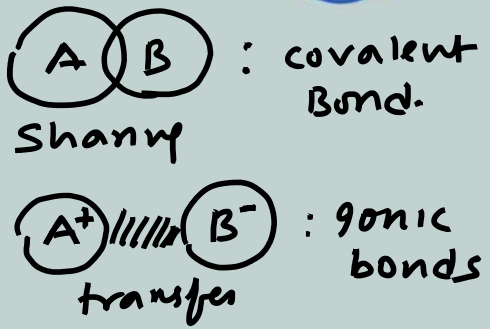
→ water has high dielectric constant than ethanol

↳ more hydration of ions.

Molecular Interactions

- Covalent (Strong)
- Non-covalent (Weak)
  - Electrostatic Interactions
  - Hydrogen Bonds
  - Hydrophobic Interactions
  - Vander walls Interactions





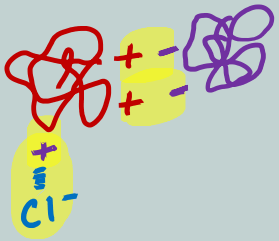
Molecular Interactions can be attractive or repulsive forces

Presence of water

Interaction	Strength (KJ/mol)
Hydrogen Bonds	12-30
Ionic interactions	6-25
Hydrophobic interactions	<40 (4-10)
Vanderwalls interactions	0.4-4.0

1. Electrostatic or ionic Interactions:

- Charge-Charge interactions/Salt bridge
- provides the highest contribution to the bio-molecule in nonpolar environment



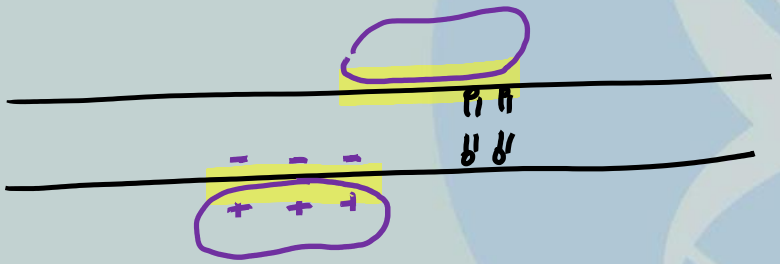
D = Low

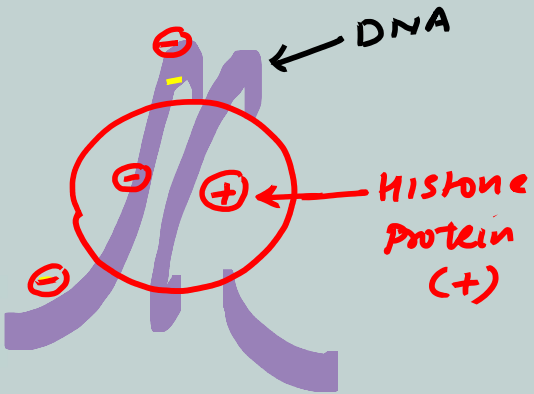
Polar env^{r} (water) D = High

Strength = ↓

Example of attractive ionic interactions

- Peripheral proteins & membrane lipids
- DNA (-) & Histone protein (+)
- Protein A & protein B

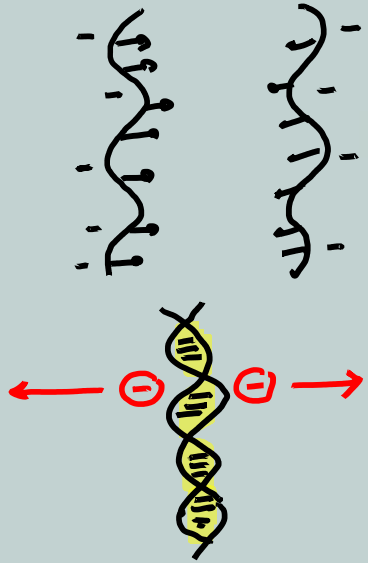




Example of repulsive ionic interactions

↳ q_1 & q_2 are having similar charge

eg Between 2 strands of DNA



- During protein folding various similar charged amino acid R-chain may come in contact with each other

Factors affecting strength of ionic interactions (6-30 KJ/mole)

1. Distance (within 4 to 10 A)

$q_1 \longleftrightarrow q_2$ $\quad E \propto \frac{1}{r}$

2. Dielectric constant of solvent

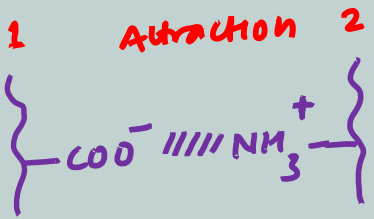
$\downarrow E \propto \frac{1}{D} \uparrow$

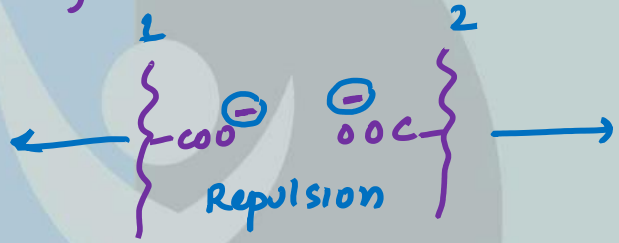
Non-polar solvent
- strong ionic bond in molecules

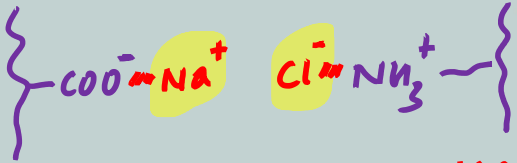
Polar solvent-
- weak ionic interaction among solutes

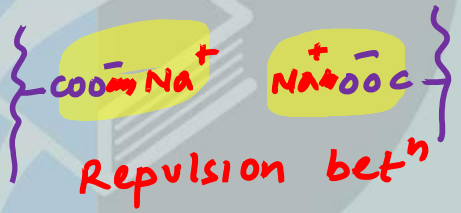
2. Salt concentration

- Decrease ionic interaction (attractive or repulsive)
- Salt ions shield charge on molecule





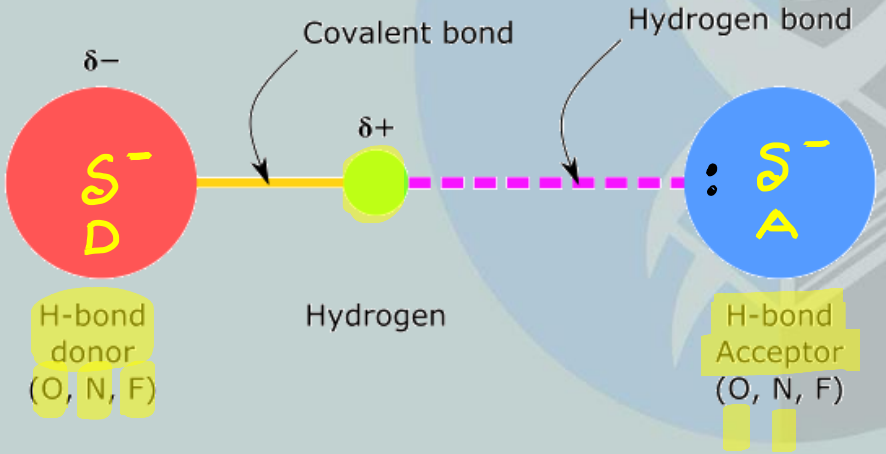




Repulsion bet^{n} molecules decreases

2. Hydrogen bond

Force of attraction between a hydrogen atom which is covalently bound to a more electronegative "donor" atom or group, and another electronegative atom bearing a lone pair of electrons—the hydrogen bond acceptor



Donor: S^- atom with covalently bound H-atom

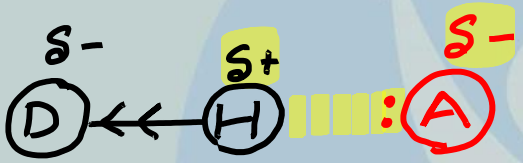
Acceptor: S^- atom with lone pair

O & N can act as donor or acceptor

What is nature of Hydrogen bond?

- 90./. ionic character
- 10./. covalent character

$$E = \frac{K q_1 q_2}{R \cdot D}$$

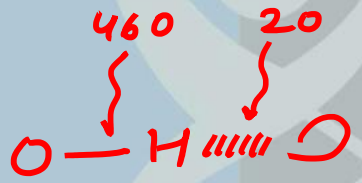


Hydrogen Bonds are very weak as compare to covalent bonds

The energy of a hydrogen bond –OH….O in water 20 kJ/mol

The energy of O-H covalent bond in water : 460 kJ/mol

Large difference



What are factor deciding strength of hydrogen bond? 12-30 KJ/mole

1. **D-H...A Angle (Linearity/ Directionality)**

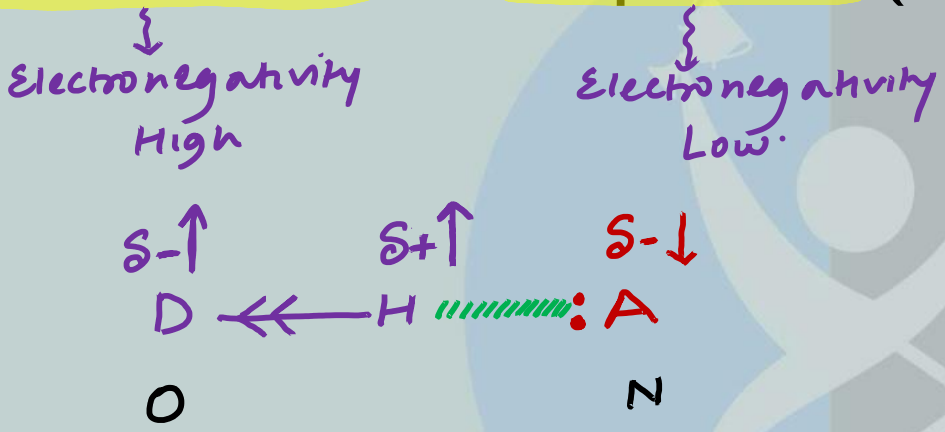
Bond angle

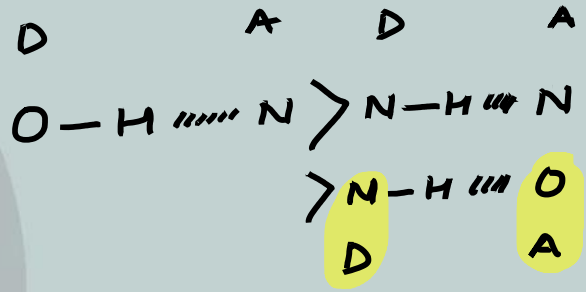
180° = strong eg H_2O, α-Helix, anti-parallel β-sheet

less than 180° = weak eg Parallel β-sheets, Double stranded DNA

What are factor deciding strength of hydrogen bond?

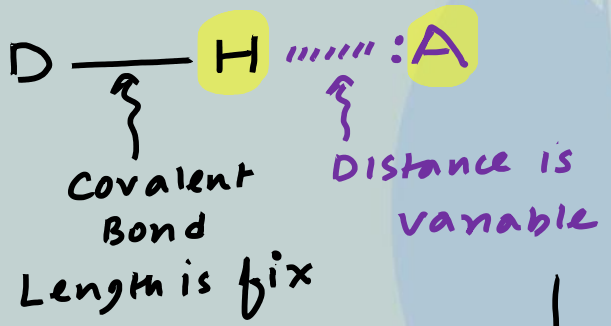
2. **Nature of donor** and **acceptor atom** (Electronegativity)

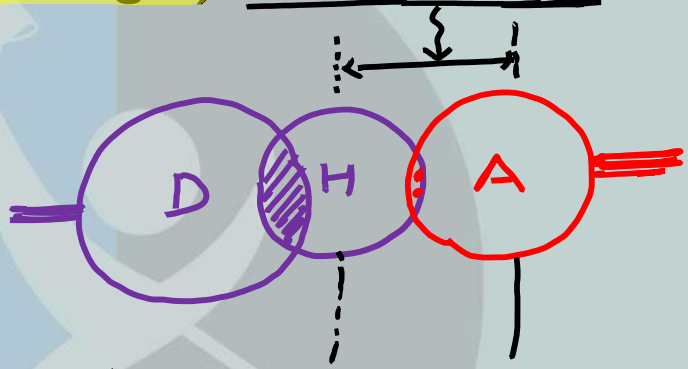


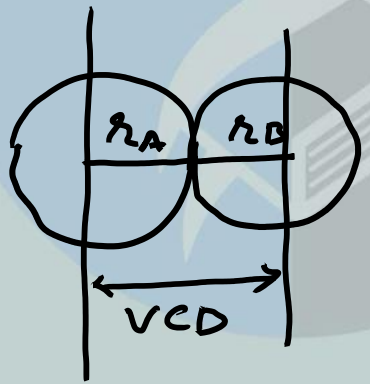


What are factor deciding strength of hydrogen bond?

3. Specific H---A distance (Bond length): Lesser than VCD







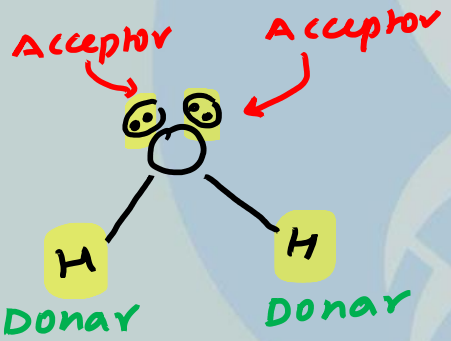
vanderwall contact distance (VCD)

Maximum number of hydrogen bonds?

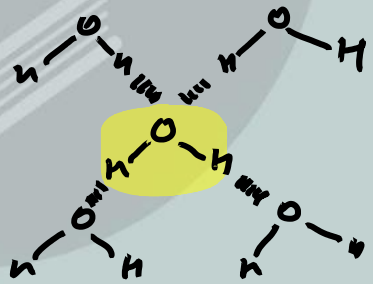
Donor position : Covalently bound H-atom to electronegative atom.

Acceptor position : Lone pairs on Acceptor atom.

eg Water



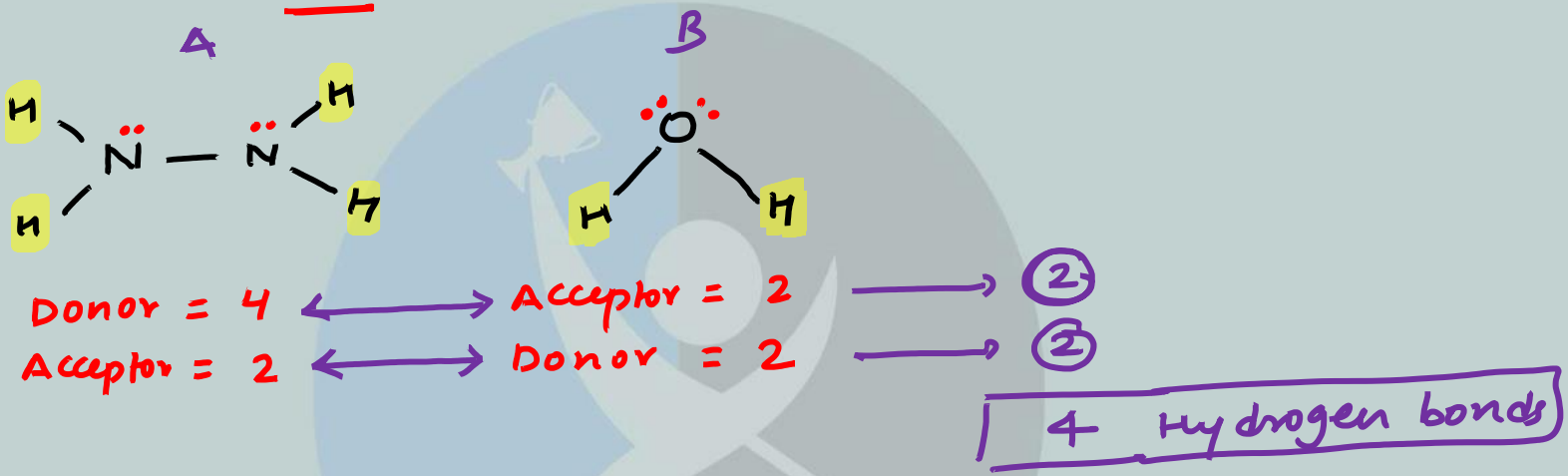
- H_2O can form maximum 4 Hydrogen bond at 0°C → Ice.



25°C : Average 3.2 H-bonds

100°C : No H-bonds.

$H_2N - NH_2$ (hydrazine) and water



G ≡ C

A = T

Why H_2O is liquid and H_2S is gas at room temperature?

able to form H- bond

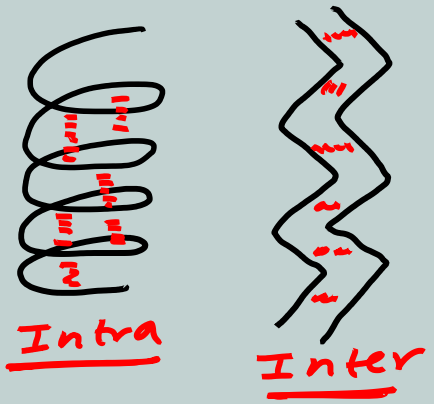
cannot form H-bond

Example of hydrogen bond in biological system

* DNA & RNA — A ≡ T or A = U; G ≡ C

* Protein : Secondary structure
  - α-Helix
  - β-sheets

* Cellulose : Inter chain H-bonding
  Starch/Glycogen : Intra chain H-bonding



Thermodynamics of hydrophilic interactions

- Solvent : Polar
- Solute : Polar
- Solution : yes

✓ ΔG = -ve

Spontaneous

Solution :

Free energy = ↓

→ Ionic interaction ✓

→ Hydrogen bonds.

Solute = Entropy = ↑

Free energy = ↑

Ionic

Hydrogen bond

The solubility of molecules in water depends on their interaction with water molecules

Ammonia > Sulphur dioxide > Carbon dioxide > Oxygen

NH_3 ⇌ $NH_4^+ + H^+$ > SO_2 > CO_2 Non-polar Linear > $O=O$ most non-polar

Solubility of gases in water

- Charged Polar (NaCl)
  - most soluble
- Uncharged Polar
  Glucose
  soluble
- non-polar eg
  lipids, O_2, CO_2
  least soluble in water

Apply Your Mind

Which of the following is not true for hydrogen bonds?

(1) They are largely electrostatic interactions ✓

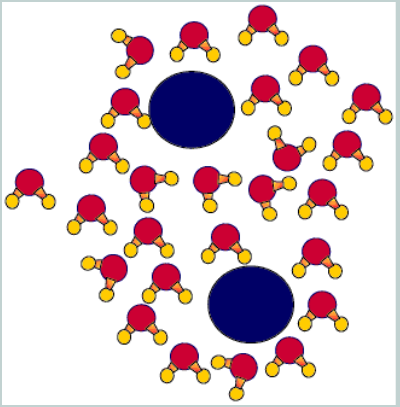
(2) They are stronger in solutes suspended in polar solvents as compare to non-polar solvents

D = ↑ weak

(3) H---A bond length is lesser than Vanderwall contact distance ✓

(4) They are directional and stronger when bond angle is 180^0 ✓

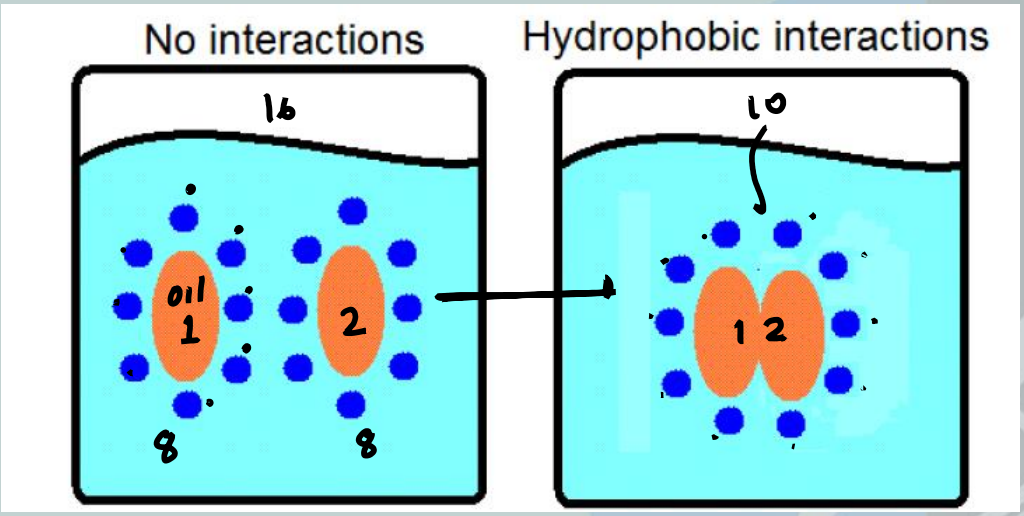
3. Hydrophobic Interactions



Tendency of non-polar substances to aggregate in an aqueous solution and to be excluded by water.

When hydrophobic substances aggregate, the water molecules around them gain entropy, which makes this process favourable.

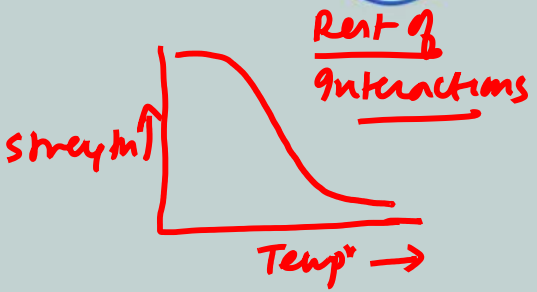
Thermodynamics of hydrophobic interactions



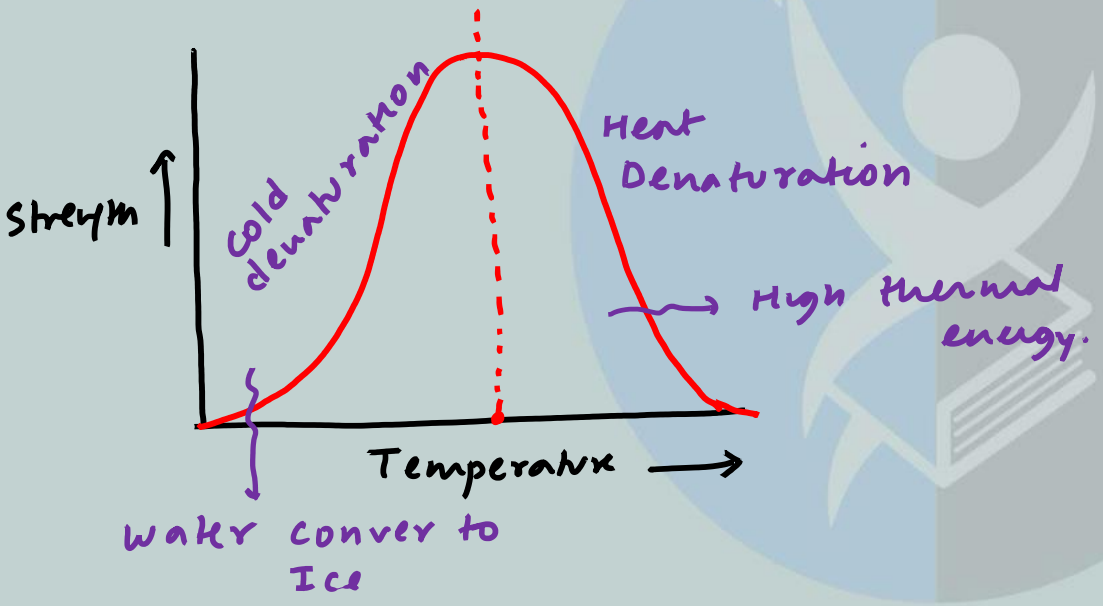
oil entropy = ↑
water entropy = ↓

oil entropy = ↓
water entropy = ↑

Factor Affecting Hydrophobic Interactions



1. Temperature



2. Chain length of Hydrocarbons.

3. Linear/branched

Linear > Branched

4. Aliphatic/aromatic

$CH_3-CH_2-CH_2-CH_2-CH_3$ > 

Aliphatic Aromatic

5. Presence of salt

Salt = ↑ (NaCl or KCl)

water effective conc^n = ↓

more solute - solute interaction = ↑

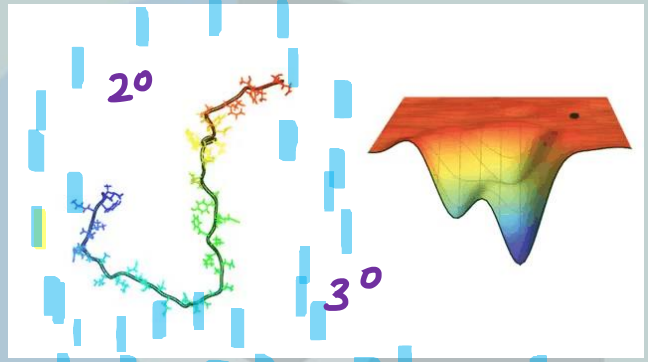
Hydrophobic interaction = ↑

eg Salting out of proteins (aggregate)

Examples of hydrophobic interactions

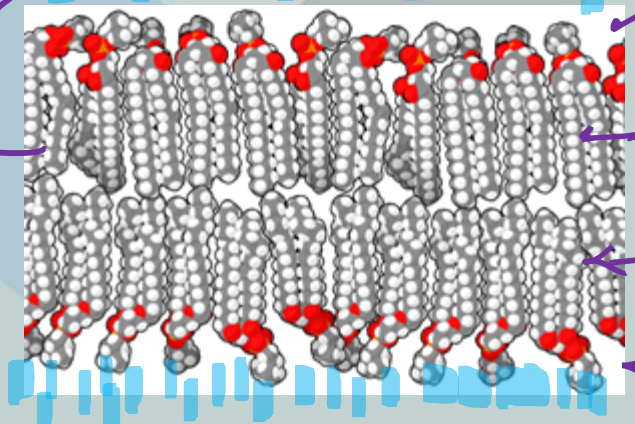
1. Protein Folding

$2^{o} \rightarrow 3^{o}$



2. Membrane Bilayer

- Non-Polar tail — Hydrophobic
- Polar Head — Hydrophilic



Apply Your Mind

Which of the following is driving force for protein folding?

(1) Covalent bonds

(2) Hydrogen bonds

(3) Vanderwalls interactions

(4) Hydrophobic interactions

$2^{o} \longrightarrow 3^{o}$

Apply Your Mind

Predominant interactions between phospholipids that stabilize a biological membrane includes

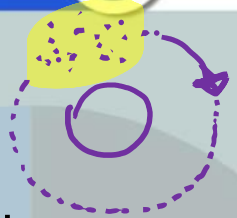
(1) Hydrophobic interactions and hydrogen bonds

(2) Hydrogen bonds and Vander walls interactions

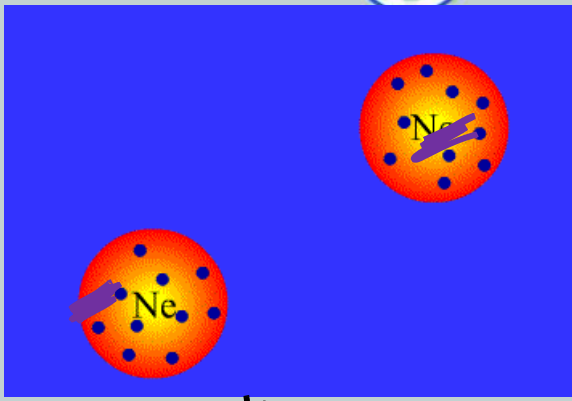
(3) Vander wall and electrostatic interactions

(4) Covalent bonds and Hydrogen bonds

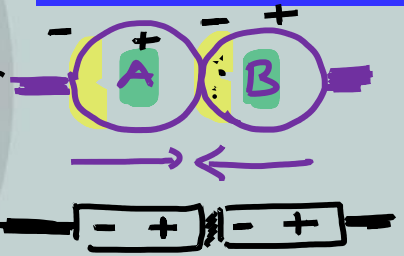
4. Vander Waals interaction:



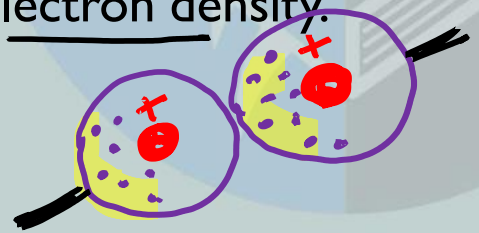
Distribution of electronic charge around an atom changes with time.



When two non-bonded atoms comes in contact with each other, they induces temporary dipoles on each other

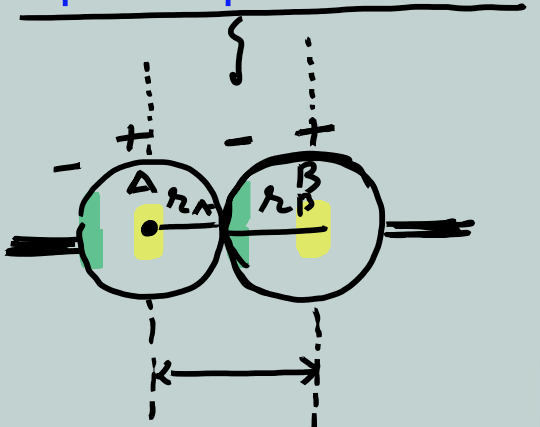


Weak attractions between molecules that result from transient fluctuations in electron density.



- Weakest ✓
- Non-specific ✓
- Most sensitive to distance ✓
- Increases with size of atoms ✓

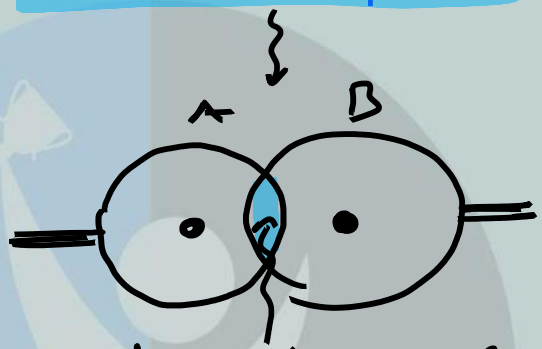
Dipole-Dipole attraction V/S Electron shell repulsion



van der waals Contact distance (VCD)

↓

Maximum attraction



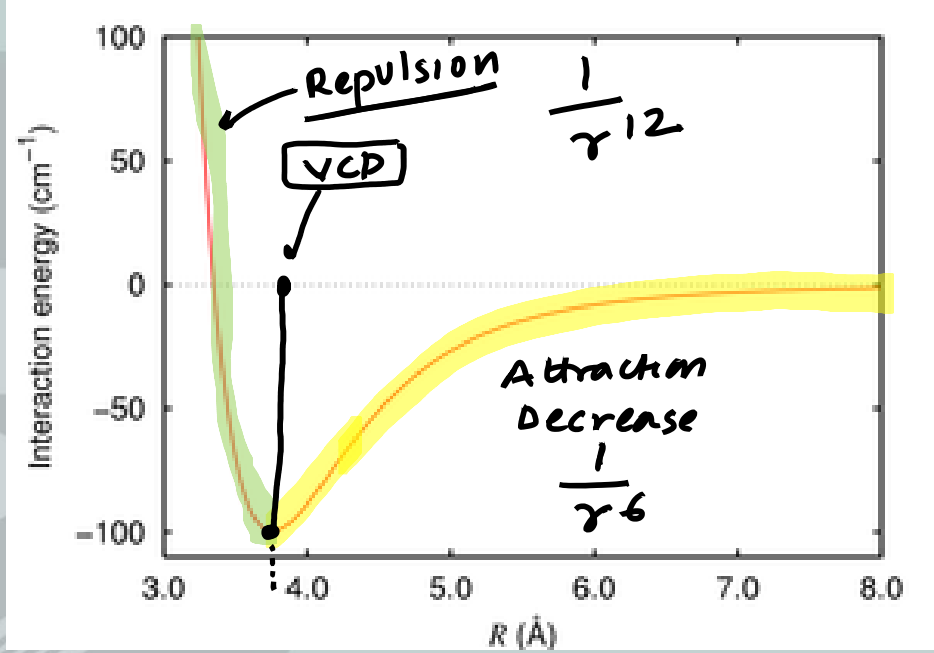
- If 2 atoms are closer than VCD strong repulsive force operates.
- due to electron shell overlapping
- steric hindrance.

van der Waals interaction

$$\Delta G_{Van} = \frac{A}{r^{12}} - \frac{B}{r^{6}} + \frac{q_1 q_2}{r}$$

repulsion Attraction

Where ΔG_{Van} is the free energy of the van der Waals interaction, A and B are constants, r is the distance between two nonbonded atoms 1 and 2 and q_1 and q_2 are partial charges on the dipoles 1 and 2. In this relation, the parameter A describes electron shell repulsion and B describes dipole-dipole attraction



Apply Your Mind

Which of the following interaction is weakest among molecules?

(1) Covalent bonds

(2) Hydrogen bonds

(3) Vanderwalls interactions

(4) Hydrophobic interctions

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